Fungi

Introduction

Fungi are **eukaryotic organisms** that possess a complete nucleus, have mitochondria, and utilize the 80s ribosome, just like human cells. Fungi have a plasma membrane similar to human cells. However, there are two key differences—ergosterol and a cell wall. The major sterol used in fungal plasma membrane is **ergosterol** rather than cholesterol. Fungi also have the ability to synthesize ergosterol in their cytoplasm. Humans rely on hepatocytes to synthesize cholesterol and LDL to circulate the cholesterol. The presence of ergosterol in the membrane is a target for treatment, as is ergosterol synthesis. Fungi also have a **cell wall**, similar to bacteria. However, the fungal cell wall is made of **chitin** and **β-glucan**, large polysaccharide molecules, very unlike the peptidoglycans of bacterial cell walls. Even though it is made from different stuff, the function of the fungal cell wall is the same as the bacterial cell wall—providing the fungus's structure and protecting it from osmotic shifts in the environment around it. Fungi are not plants and cannot perform photosynthesis. Fungi **eat plants**—often found on rotting vegetation or in the soil. Fungi are ubiquitous and facilitate decomposition. They are the great recyclers, crucial for the environment's homeostasis. We don't want to see them from the perspective of nature, but rather from the perspective of anti-human. That is because fungi also eat us. If a fungus invades your body and evades your immune system, that fungus can use your human cells for food. That's what causes disease.

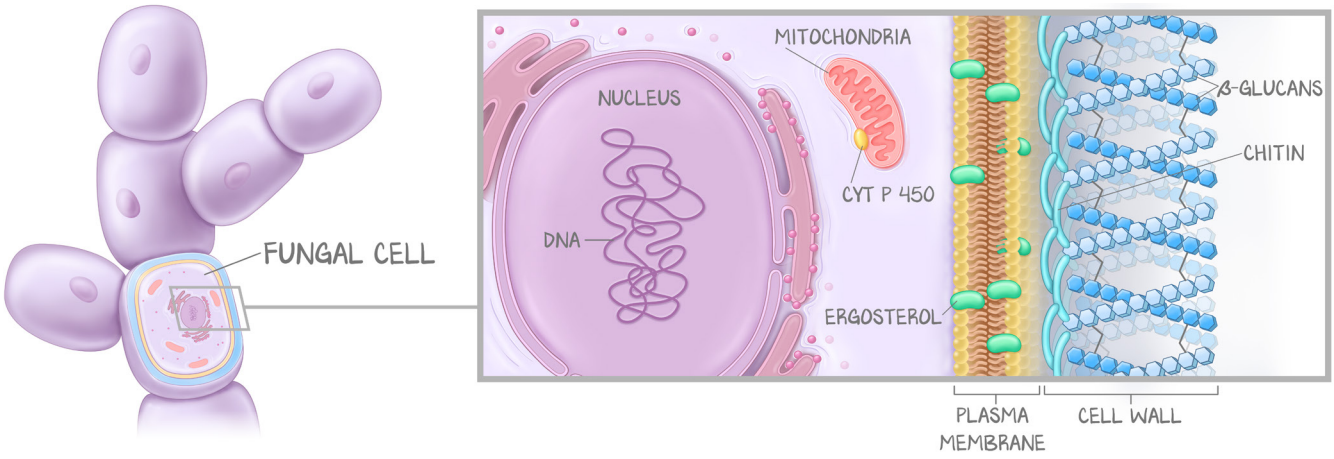


Figure 1.1: Fungi
A fungal cell is eukaryotic, sharing many similarities with human cells. There is a proper nucleus, double-stranded DNA, and membrane-bound organelles, including mitochondria. The cell is lined by a plasma membrane, a lipid bilayer, also like human cells. However, the plasma membrane of fungal cells utilizes ergosterol rather than cholesterol, and every fungal cell has the ability to synthesize its own ergosterol. More akin to prokaryotic bacteria, fungal cells also possess a cell wall. Fungal cell walls are made of chitin and β-glucans.

Histologically, fungi can be found in one of two forms—yeasts or molds. The **yeast** form is a single-celled, round to oval fungus. Yeasts undergo budding, the fungal equivalent of bacterial cell division, the asexual production of a genetically identical clone; one yeast becomes two. The **mold** form consists of hyphae (sing. hypha)—long tube-like structures. Hyphae reproduce by making spores which are released into the air. Some organisms can go between a yeast form and a mold form, and are called **dimorphic**. Most dimorphic organisms are thermally dimorphic, the temperature of their environment dictating the form they take. Remember the phrase, "*dimorphic fungi are mold in the cold*," where "the cold" means the temperature of the environment outside the warmth of a human being. In the environment and on fungal culture (22°C), a thermally dimorphic fungus will be a mold. When the mold form of the fungus gets into a human, where it is warm (37°C), the mold becomes a yeast. The yeast form causes disease by eating human cells. The dimorphic fungi of import are *Histoplasma*, *Blastomycoses*, *Coccidioides*, and *Sporothrix*.

Hyphae are the filamentous cellular units of molds. Hyphae can be septate or nonseptate. **Nonseptate** hyphae have no cross walls and are usually irregular in width, are large, and have a **broad angle of branching.** Nonseptate hyphae are illustrated by *Mucor*, below. **Septate** hyphae have **cross walls**, their width is generally consistent, and they have branches that occur at large angles. Septate hyphae are illustrated by *Aspergillus*, below. *Candida albicans* can form **pseudohyphae**, which appear similar to septate hyphae except that the consistency of the tube width is interrupted by small pinched regions and there are no complete cross walls. This is discussed in detail below.

Spores are how fungi multiply. They are the asexual production of a new fungus. Conidia (sing. conidium) are made off an existing hypha and are released into the air. Arthroconidia are spores within the hypha that do not distend the hypha membrane. Spherules are packages of spores contained by a membrane. Blastoconidia are the budding spores of yeasts. Spores are how fungi multiply and spread.

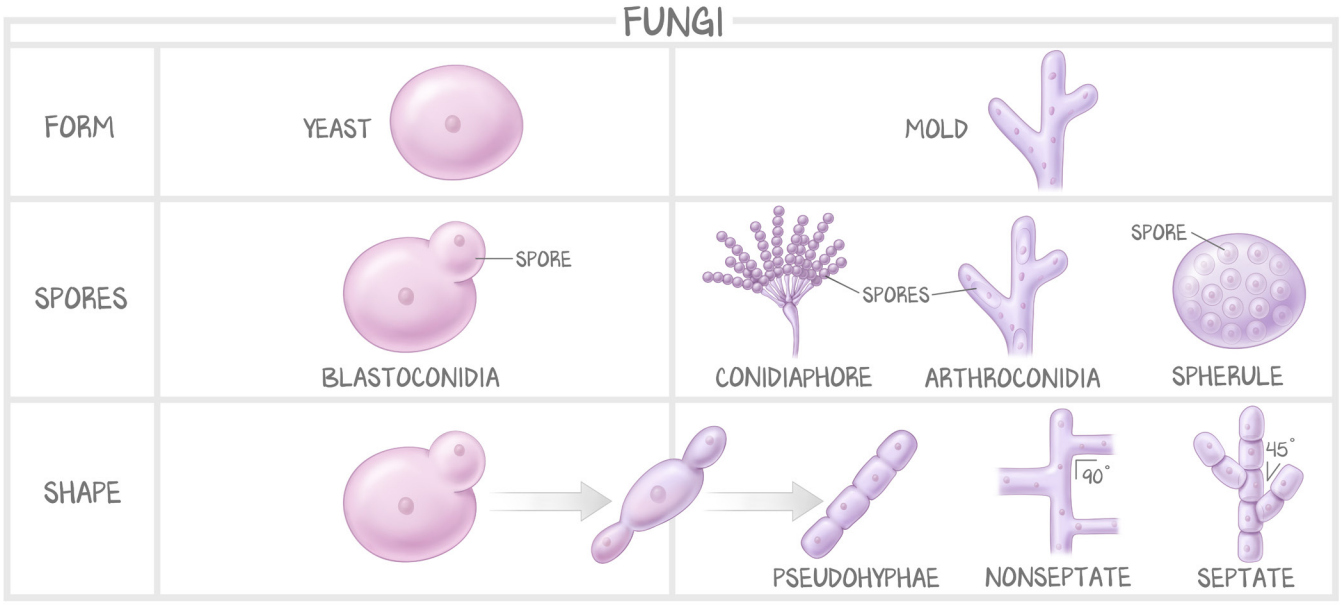


Figure 1.2: Fungal Structures
Artistic rendering of the various forms fungi can take. When evaluating the slides of actual fungi later in this lesson, refer back to this image to orient you as to what you should be looking for.

Diagnosis is made visually, by culturing the organism, and by various antigen detection or immunofluorescence. To grow fungus, a special fungal culture must be used: **Sabouraud agar**. Fungal cultures grow much slower than bacterial cultures and can take weeks to turn positive. When tissue samples contain fungus (used particularly in skin scrapings and vaginal secretions), using a **KOH prep** on the microscope slide will facilitate the removal of human cells, revealing only the fungus on the slide. Most fungi are colorless. **Lactophenol blue** can make the fungus easier to visualize under a microscope. Other special stains can be used to make specific organisms more visible. We discuss the specific stains for specific bugs in line with the bugs.

This lesson will cover all clinically relevant fungi. While we mention treatment in this lesson, the discussion of antifungals is reserved for the next lesson. We start with those that cause superficial infections, mild disease—the cutaneous fungi and *Sporothrix*—then transition to the dimorphic systemic fungi—*Histoplasma*, *Blastomyces*, and *Coccidioides*. The bulk of the lesson revolves around the fungi that cause disease only in immunocompromised patients, the opportunistic fungi—*Candida albicans*, *Aspergillus*, *Pneumocystis*, *Cryptococcus,* and *Mucor/Rhizopus*.

Cutaneous Fungi

On skin. *Malassezia furfur* causes the disease **tinea versicolor**. The fungus lives in the most superficial layer of the epidermis, on and in the keratin of skin. Where infected, the skin will appear as hypopigmented patches. Scrapings of the hypopigmented regions will ensure that organisms are obtained. Applying KOH removes human skin cells. What is revealed is what is referred to as **spaghetti and meatballs**, a product of yeast clusters and short curved septate hyphae. A **Wood's lamp** can be used to make the diagnosis as well. Treat with selenium shampoo (normally used for dandruff of the scalp) on the skin of affected areas.

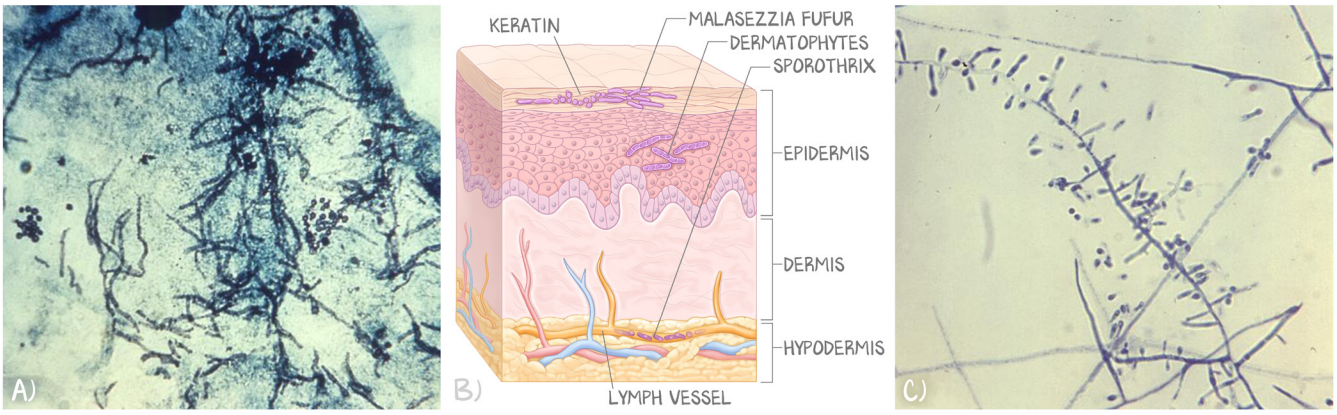


Figure 1.3: Skin Fungi
(a) An example of *Malassezia furfur*—a combination of round spores (the "meatballs") and elongated, broken pseudohyphae (the "spaghetti"). (b) The location of the cutaneous fungi. *Malassezia* is the most superficial, within the stratum corneum. The dermatophytes are amongst the keratinocytes beneath the keratin barrier. *Sporothrix* is deep, past the dermis, in the lymphatics. (c) An example of a KOH prep of skin scrapings demonstrating *Trichophyton*.

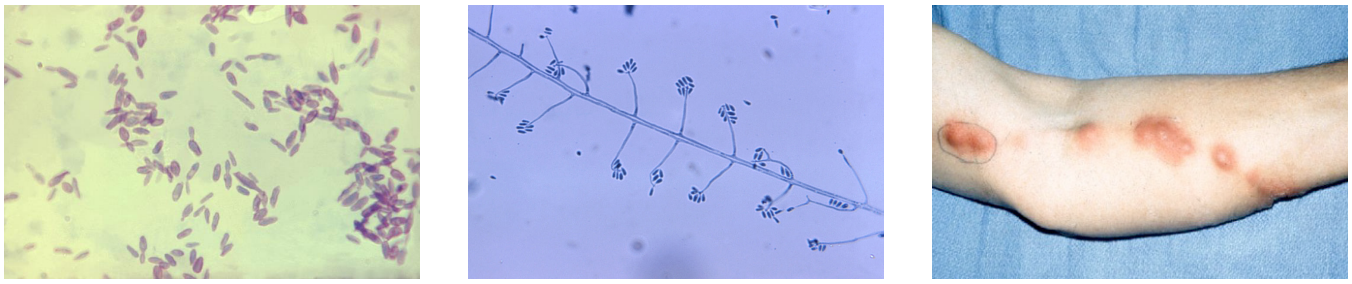
In skin. Dermatophytes (*Trichophyton, Epidermophyton, Microsporum*) infect skin, hair, and nails. Trichophyton can infect all three (tri-chophyton). Epidermophyton affects nails and skin only, but not hair. The other one, *Microsporum*, infects hair and skin, but not nails. Dermatophytes live in the epidermis, beneath the keratin but above the stratum basale. They live within the epithelium with the keratinocytes. They are referred to as ringworms because they cause circular lesions on the skin. They are NOT worms (helminths). They are fungi. Dermatophyte infections are termed "tineas." The disease they cause is named by the location they are infecting. Tinea capitis is on the head, tinea corpus is on the body, tinea barbae is on the beard, tinea pedis is athlete's foot, tinea cruris is jock itch, and tinea unguium is on the nails. Patients will present with itchy, scaly lesions of skin affected or well-circumscribed hyperpigmented patches. The only thing that matters is **if the nail is infected, then long-term oral antifungals** (terbinafine, imidazoles) are required. If the nail is not infected, **topical imidazoles** (powders, creams, sprays) are all that are needed, each equivalent to the other. Keep the areas being treated dry. Skin scrapings are generally not required, but if performed, will reveal arthroconidia.

Lymphatics Fungi

Sporothrix. *Sporotrichosis* is known as **rose gardener's disease**. *Sporothrix* lives in soil (garden). When the skin is punctured by a fungus-contaminated material (the thorn of a rose bush), the fungus is introduced into the hypodermis where lymphatics are. The fungus gets into lymphatics and ascends. The effect on the skin is **ulceration**. A nodule appears first, then ulceration follows. Lesions first appear at the site of penetration, then progressive ulcerations will occur following the route of the lymphatic chain. *Sporothrix* is thermally dimorphic. When cultured at room temperature, it is "mold in the cold,"

presenting with **daisy-cluster hyphae**, hyphae with oval conidia in rosette-like clusters. If a sample is taken from a human, KOH is applied to remove the human tissue, and *Sporothrix* appears in the yeast form, described as **cigar-shaped yeasts**. Treatment is to ingest potassium iodide with milk and to apply potassium iodide to the lesions. The patient can also take itraconazole instead.

Because the systemic dimorphic fungi that cause pneumonia (coming next) are treated with itraconazole, it is safe for you to learn that "dimorphic fungi are treated with itraconazole." However, if you have the brain space, *Sporothrix* gets potassium iodide (KI), and pneumonia-causing dimorphic fungi get itraconazole.



(a) (b) (c)

Figure 1.4: *Sporothrix*
(a) The yeast form of *Sporothrix* is elongated and cigar-shaped. This is the form *Sporothrix* takes in humans. (b) The mold form of *Sporothrix* is found on a fungal culture, grown at room temperature. The mold form is known as daisy-cluster hyphae, clusters at the end of a slender projection. (c) The cutaneous manifestations of sporotrichosis. Ascension of the fungus up the lymphatics leads to nodules that ulcerate.

Dimorphic Systemic Fungi

The "systemic fungi" are actually "pulmonary fungi." Only if the host becomes profoundly immunocompromised do these fungi actually go systemic. If systemic, or rather, disseminated, they need to be treated with amphotericin B. If they are contained to the lung, they are treated with **itraconazole**.

These dimorphic systemic fungi are all thermally **dimorphic**, and so are "mold in the cold." They live **in the soil**. Each has a unique mechanism for producing spores, which we will discuss. The purpose is always the same—to spread their spores into the air. They live in soil, producing spores. Then, a human does something that disrupts the soil, flings the spores into the air, and inhales them. When they get into the warmth of the human body, they become **yeasts in humans**. Those spores were inhaled into the lungs. For an immunocompetent patient, there are two outcomes—asymptomatic (almost everyone) or pneumonia. Even when the presentation is pneumonia, the pneumonia is mild and self-resolving. The patient never knows they had a fungal pneumonia.

For each fungus, there is an endemic area of the United States, a behavioral risk factor, and a yeast form histologic finding that is pathognomonic. Some other details are sprinkled in that we think you should associate with that fungus. A person who lives in an endemic region is used to the fungus, so cannot get acute disease. People who **travel to an endemic region** and do something to expose themselves to fungus can get pulmonary symptoms. People who **live in an endemic region** likely have the fungus. They don't get the acute disease but become colonized. Exposure to an endemic area needs to be considered when starting immunosuppressants. The patient may never have had any symptoms. But take away their immune system, and the fungus rages. See these three fungi like TB—they cause pulmonary disease, live in humans dormant if ever exposed, immunosuppression releases them, and they have skin tests to assess exposure. The major difference is that they do not cause cavitary lesions and are not contagious like TB is.

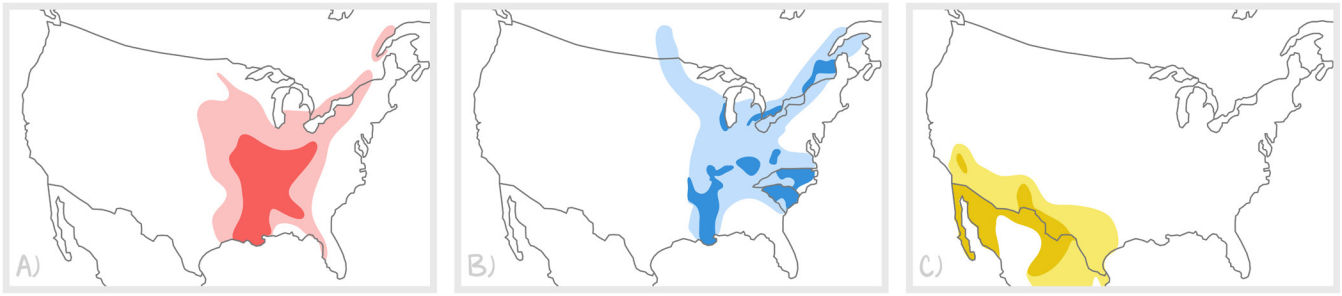
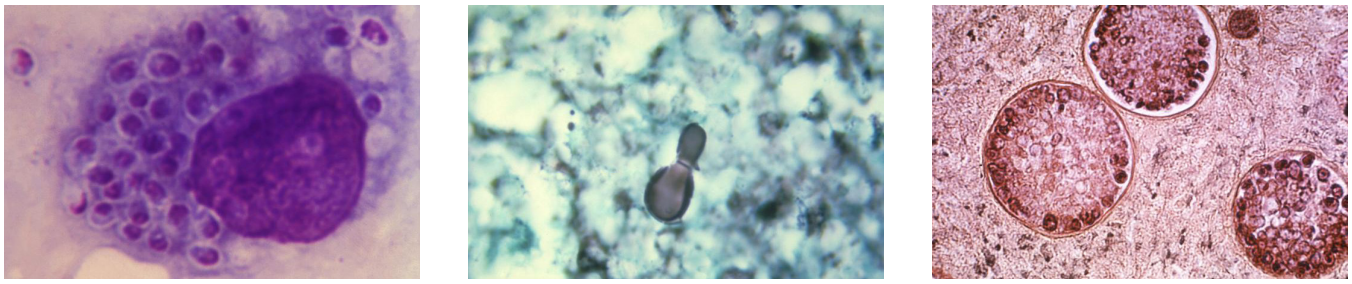


Figure 1.5: Endemic Comparison of Systemic Fungi
(a) *Histoplasma* has the highest density in the Ohio River and Mississippi River valleys. (b) *Blastomycoses* is also found in a similar distribution to *Histoplasma*, but with a high concentration in the Carolinas and with more spread into Canada around the Great Lakes. (c) *Coccidioides* is found in the southwest United States and Mexico, the dry, arid desert regions.

Histoplasma. "*Histo*" is endemic to the Mississippi and Ohio River valleys. We use "farms and fields" as memory cues for histoplasma. *Histo* is found in **soil** but is inhaled into the lungs to cause disease. *Histo* lives in soil. Soil enriched by bird droppings lets *Histo* grow and multiply. Humans do something to kick up the soil and send the moldy *Histo* into the air to be inhaled. "Farms and fields" is used to remember that *Histo* is associated with cleaning **chicken coops** or **bulldozing barns**. "Farms and fields" is also used in contrast to *Blasto*, discussed next. *Histo* doesn't discriminate between flying mammals, as long as those mammals provide nutrients. "Histo" is also the pulmonary infection associated with cave exploring, **spelunking.** In caves, bat-dropping-enriched soil causes *Histo* to grow. Humans doing the exploring kick up the soil. Identifying *Histoplasma* is often done within a human sample rather than by culturing it. The yeast is **facultatively intracellular** and very small. *Histoplasma* is found **within macrophages**. It is the only fungus that we discuss to do this, and the finding is pathognomonic. On a fungal culture, it is mold in the cold, and will present with hyphae, microconidia, and tuberculate macroconidia—distinct features, but not nearly as important as the yeast form in macrophages. Amphotericin B if disseminated, itraconazole if pulmonary, though often no treatment is required.



(a) (b) (c)

Figure 1.6: Dimorphic Fungi Diagnosis
(a) *Histoplasma* is visualized as intracellular yeasts within macrophages. (b) *Blastomycoses* is visualized by its alliteration—broad-based budding yeasts. (c) *Coccidioides* is visualized with endospores contained in spherules.

Blastomycoses. "*Blasto*" has a near-identical endemic region as *Histo*, yet you will be tasked with separating them based on endemic region and risk factors. *Blasto* has a greater reach than *Histo*, its endemic area including Canada near the great lakes and the eastern coastline of the US. And instead of chicken coops and spelunking, *Blasto* is associated with **beaver dams** and **rotting wood**, being associated with "woodlands and streams" rather than "farms and fields." Woodlands reminds you of rotting wood, streams of the beavers who use wood to build dams in streams. *Blasto* starts as an acute pulmonary disease. Unlike *Histo*, even in immunocompetent patients, *Blasto* causes a fungal pneumonia that does require treatment. In AIDS patients, it will disseminate, where it causes **verrucous skin lesions** that resemble squamous cell carcinoma. B*lasto* can be identified by its **broad based budding yeasts**, the form

it takes while inside us. The culture form of *Blasto*, the mold has no distinct form. Local pulmonary disease is treated with itraconazole. Disseminated disease is treated with amphotericin B.

Coccidioides. "Coxidio" is the dimorphic fungus that causes San Joaquin fever. The San Joaquin Valley is located in the southwest United States, from which the disease gets its name. But do not be misled. It is not the entire valley that predisposes the patient to infection, but rather the very most southern parts of the valley - the dry arid desert of California, Arizona, Texas, and Mexico. *Coccidioides*, like *Histo*, presents in immunocompetent patients as a self-resolving pneumonia. You can see desert nodules on the skin during the infection. Pulmonary lesions tend to calcify. The fungus is found in the environment and on culture as "mold in the cold," presenting with arthroconidia. In humans, the yeast form is seen with **spherules**. If you see a spherule you have made the diagnosis. Like *Histo*, *Coccidioides* often does not need treatment for immunocompetent patients, though itraconazole can be used if needed. If *Coccidioides* disseminates (AIDS immunocompromise), just as the other dimorphic fungi, amphotericin B is required.

ORGANISM	ENDEMIC REGION	PATH	FEATURES
Histoplasma	Mississippi and Ohio River valleys, fields and farms	Intracellular yeasts within macrophages	Bird or bat droppings Diagnose with urine antigen
Blastomycoses	*Histo* + Canada, East Coast Woodlands and streams	Broad-based budding yeasts	Verrucous skin lesions that can mimic SCC
Coccidioides	Southwestern US, arid, deserts	Spherules on yeast	

Table 1.1: Dimorphic Systemic Fungi Review

Opportunistic Fungi

Opportunistic fungi fail to induce disease in most immunocompetent people, but do induce disease in people with **impaired host defenses**. Some of the following fungi cause one disease and have one risk factor that should be associated with that disease. Other fungi cause multiple diseases, and the risk factor for one disease is different than the risk factor for another. For example, *Candida* in the blood (candidemia) is associated with central venous access and the administration of total parenteral nutrition (TPN), while *Candida* in the vagina (vulvovaginitis) is associated with corticosteroid use. In general, people who suffer from opportunistic infections are immunocompromised. The remainder of these organisms exist only in one form. The exception is *Candida albicans*.

Candida albicans. *Candida* is a **pleomorphic** fungus with at least three histologic forms. It is NOT thermally dimorphic and does NOT follow "mold in the cold." In culture, in the cold, outside of humans, *Candida albicans* forms an **oval yeast**. Humans get infected by *Candida albicans* and in humans, in the warmth of our body, it grows the **mold** form. *Candida albicans* in mold form grows **pseudohyphae.** *Candida albicans* can also grow true hyphae when it invades (other *Candida* species cannot). You should stay focused on pseudohyphae as the buzzword for *Candida*. Pseudohyphae are a product of incomplete budding. *Candida albicans* is an oval yeast. It forms budding conidia when an oval yeast. In humans, those oval yeasts elongate as they bud. The elongation gives the appearance of a hypha, and the next budding gives rise to a bud at the tip of that "hypha." That bud almost completes budding, but stays connected to the yeast that made it. Then the bud elongates and generates its own bud. The chain of elongated buds gives the appearance of septate hyphae—long tube-like structures with obvious separations along the length—but aren't actually septate hyphae. The things that look like cross-walls are actually the separation of two organisms, their plasma membranes. The key morphologic distinction is that where the "hyphae cross-wall" exists, there is a little pinch of what should be a smooth tube.

A confirmatory test for *Candida albicans* is to incubate it at **37°C** in serum where those oval yeasts grow **germ tubes**. A germ tube is the oval yeast budding and elongating, changing its appearance from a circle to an elongated pseudohypha.

Candida albicans is part of the **normal human flora** of mucous membranes—the oropharynx and the vagina. When a patient gets a little immunocompromised (diabetes, antibiotics, or steroids) *Candida albicans* can **overgrow**, causing disease. **Oral thrush** is overgrowth in the mouth. Thrush presents as a thick white cottage cheese that is easily scraped from the mucosa of the mouth. It can be treated with nystatin (swish and spit) or with clotrimazole troches. **Vulvovaginal** candidiasis presents as a thick white cottage cheese that is easily removed from the wall of the vagina. Diabetes and antibiotic use for UTIs (which kill off other nascent bacteria, allowing the *Candida* to grow in the vagina) are risk factors. Treat with either a single oral dose of fluconazole or clotrimazole topically. **Cutaneous** candidiasis occurs in regions of skin that are not well aired out, those that create a moist and warm environment. This happens in skin folds and up against wet diapers. It happens to pudgy babies when it's hot, obese patients all the time, and to nonobese babies' diapers. Keeping the area dry and treating with topical imidazoles is sufficient.

When a patient gets seriously immunocompromised (AIDS, burn victims, long-term hospitalizations), *Candida albicans* can **invade**. Invasion requires more aggressive treatment. **Esophageal** candidiasis is an **AIDS-defining lesion** that presents with dysphagia. It is treated with oral fluconazole or nystatin swish and swallow. A bloodstream infection with *Candida* (**candidemia**) is associated with long-term central venous catheters, especially those patients receiving TPN. This requires removal of the plastic tubing and micafungin (or amphotericin B). In patients who are **neutropenic** (an absolute neutrophil count < 500) and are **febrile**, but no causative organism can be identified and antibacterials attempted, *Candida albicans* becomes the presumed infection, treated with caspofungin.

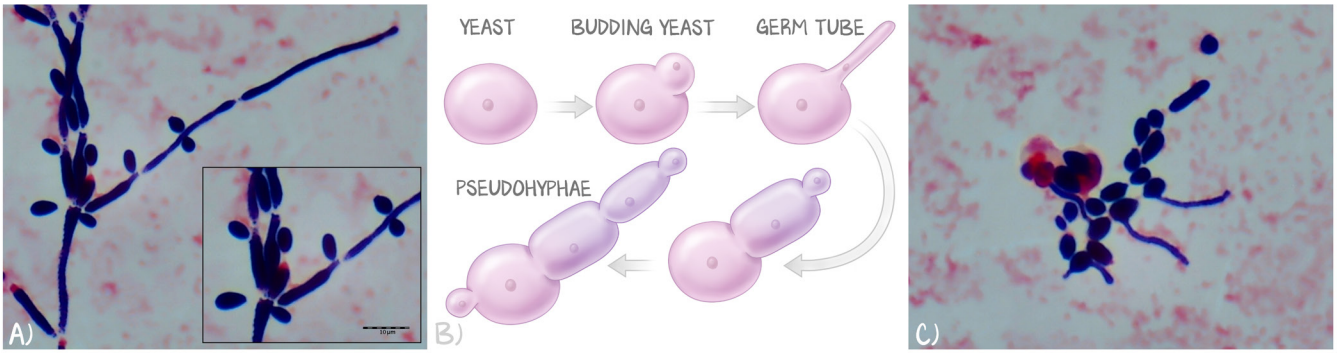


Figure 1.7: *Candida albicans*
(a) The pseudohyphae of *Candida albicans* with new budding yeasts. (b) Artist's rendition of the transformation of *Candida* from an obvious yeast-looking fungus when not at body temperature, into the pseudohyphae structure commonly associated with *Candida* infections in humans. As the yeast buds, the bud elongates. The initial budding-and-elongating is known as a germ tube. The process repeats until pseudohyphae form. (c) An example of germ tube formation, round yeasts with elongated projections that will become pseudohyphae.

Aspergillus. *Aspergillus* exists only as a **mold**. *Aspergillus* can be diagnosed simply on a KOH prep, revealing **septate hyphae** that branch at **45° angles**, giving rise to **V-shaped** branches. Spores form at the ends of hyphae in **radiating chains**. *Aspergillus* grows on decaying vegetation and releases its spores into the air, which we then **inhale**. The diseases *Aspergillus* causes, therefore, are primarily pulmonary. There are three—ABPA, aspergilloma (aka fungus ball), and invasive aspergillosis. Associate **voriconazole** with the treatment of *Aspergillus* infections. The only indication for voriconazole is *Aspergillus*. *Aspergillus* does not get amphotericin B.

Allergic bronchopulmonary aspergillosis (ABPA) is NOT an infection of *Aspergillus*, but rather a **hypersensitivity reaction** to the presence of *Aspergillus*. Commonly seen in patients with cystic fibrosis (growing in mucous plugs but not invading lung tissue), it presents like asthma—wheezing, dyspnea, eosinophilia—unresponsive to medical therapy. The **eosinophilia** is misleading, as asthma does present with eosinophilia. But the eosinophilia is because of the *Aspergillus*, which can be confirmed with **IgE** against *Aspergillus* antigens. Treat the patient with corticosteroids (for inflammation) and voriconazole (for the *Aspergillus*).

Aspergillomas grow in pre-existing cavitary lung lesions, such as are made by previous lung abscesses or TB. The aspergilloma, called a fungus ball, can be seen on CT scan of the chest. There will be a mass within an old cavitary lesion. *Aspergillus* likes to bore into the lung, which can result in pulmonary hemorrhage. Surgical resection reduces coughing and decreases risk of pulmonary hemorrhage. Voriconazole is used to treat aspergillomas.

Invasive aspergillosis occurs only in the immunocompromised. *Aspergillus* may disseminate, but the symptoms of invasive aspergillosis still focus on the lung, presenting with fever, hemoptysis, and chest pain. A CT scan of the chest shows a **halo effect**, an intense bright signal surrounding ground-glass opacities. Invasive aspergillosis is treated with voriconazole.

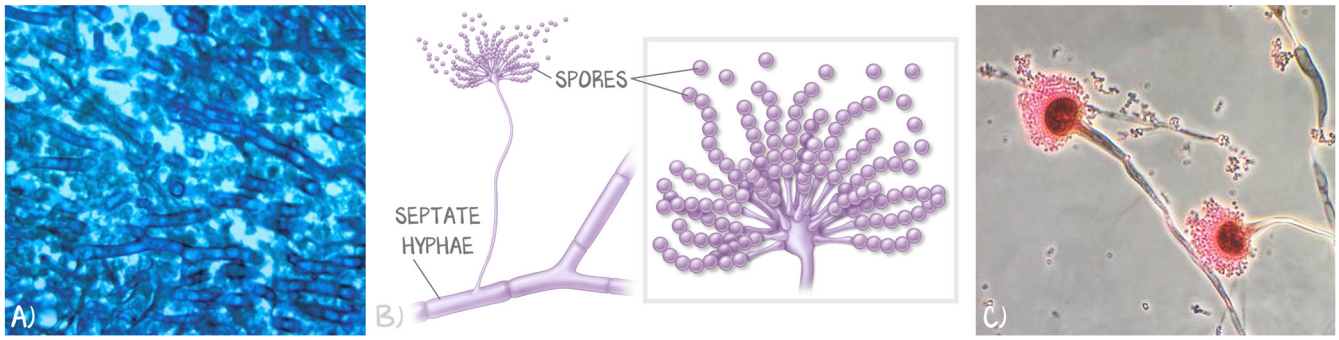


Figure 1.8: *Aspergillus*
(a) The septate hyphae of *Aspergillus* and the narrow branching angles, as seen at 8 o'clock. (b)Septate hyphae, the long thin stems on which the conidiophores arise. (c) A close-up demonstrating two conidiophores arising from a well-defined "foot cell" and terminated by a swollen vesicle bearing flask-shaped chains of spores.

Pneumocystis. "PCP" is a **disc-shaped yeast** that is **inhaled** into the lungs and causes **pneumonia** in **AIDS** patients. It is named *Pneumocystis jirovecii* and was formerly named *Pneumocystis carinii*. Since the disease it causes is a Pneumocystis pneumonia, "PCP" stuck as shorthand. Now the organism is referred to as "PCP." The patient will have a CD4 count < 200, present with an **interstitial pneumonia** (no consolidation, but diffuse white-out on X-ray; ground-glass opacities on CT scan), and be hypoxemic. The diagnosis is made by **silver stain** of a sample of induced sputum, identifying the yeast. A Giemsa stain can also stain them positive, but you should be choosing silver stain. In patients that cannot deliver a sufficient sample or who are already intubated, bronchiolar lavage is sufficient to make the diagnosis. Treatment is with **intravenous TMP/SMX** (not an antifungal). Prophylaxis against PCP is started for patients with CD4 counts less than 200 with **oral TMP/SMX**. If TMP/SMX is not tolerated, then dapsone is used for prophylaxis. If dapsone is not tolerated, prophylaxis is achieved with atovaquone.

***Cryptococcus*.** "Crypto" exists only as a **yeast**. It is round, forms narrow buds, and has a **very thick polysaccharide capsule**. *Crypto*, like other fungi, is inhaled through the lungs, so can cause a pneumonia. However, you should associate *Cryptococcus* with meningitis. **Cryptococcal meningitis** occurs in AIDS patients (CD4 is usually less than 100), presenting as **fever and a headache**, often accompanied by

seizure. A lumbar puncture will reveal very high opening pressures. If left untreated, the increased intracranial pressures will herniate the brain. The current best method for making the diagnosis of cryptococcal meningitis is **cryptococcal antigen in CSF** (called a CSF latex agglutination test, cryptococcal capsular antigen test, or CrAg). The culture and stain are not needed to make the diagnosis nor to start treatment. Treatment is with **amphotericin B and flucytosine** together for two weeks (induction phase), followed by a long course of fluconazole oral therapy (maintenance phase). *Crypto* is easily visualized on the **India ink** stain. India ink is black or dark brown. It stains everything except the fungus because of its capsule, causing the white circular organism to stand out against the dark background. You should also be aware of **mucicarmine stain**, which stains *Crypto* red. Neither stain is the preferred method of diagnosis, but you should be able to identify *Crypto* on either stain (Figure 1.9).

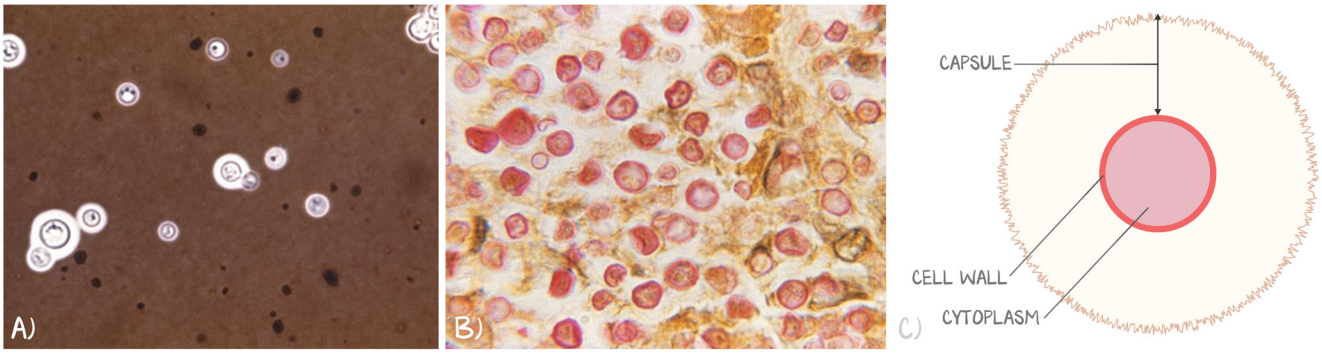


Figure 1.9: *Cryptococcus*
(a) *Cryptococcus* as seen on India ink. The dark brown (sometimes black) background highlights the white fungus, which does not take up the stain. The central dark ring on each yeast represents the end of the cell and the start of the capsule. (b) Mucicarmine stain stains the cell red, leaving the white capsule surrounding the red cell. The brown is merely background. (c) Artist's depiction demonstrating the massive size of the capsule relative to the cell's size.

***Mucor* and *Rhizopus*.** "*Mucor*" exists only as a **mold**. It possesses the quintessential **nonseptate hyphae** with **wide** and irregularly shaped tubes. It exhibits **wide-angle branching** that approaches **90°**. The spores are stored in a **sporangium** (a containment of spores like an endospore, but at the end of a hypha like a conidium). These fungi are associated with **diabetic ketoacidosis** and with the **rhinocerebral infection** (sinuses and brain) formerly known as mucormycosis. They grow in the ground, get into the nasopharynx through inhalation, then begin growing without respect for anatomical barriers, boring through the nasopharynx into the brain. The treatment is emergent debridement and amphotericin B. These are highly fatal even when treated.

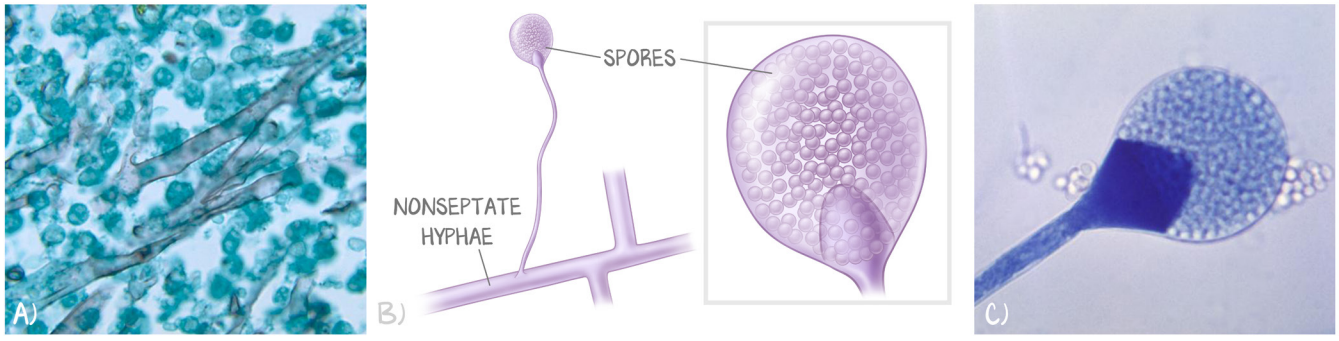


Figure 1.10: Mucor and Rhizopus
(a) While branching isn't clearly seen, the absence of cross-walls (nonseptate hyphae) is shown clearly. (b) Artist's rendition for orientation, showing both the nonseptate hyphae and the globular sporangium supported by a column-shaped columella. (c) A close-up of the sporangium, visualizing the sporangiospores within.

BUG	IDENTIFICATION	TREATMENT	SYMPTOMS	ASSOCIATIONS
Candida albicans	Pseudohyphae Germ tubes at 37°C	Nystatin swish	Oral thrush	Inhaled steroids
		Topical azole	Cutaneous	Obesity
		Fluconazole	Vulvovaginitis	Antibiotics, DM
		Caspofungin	Neutropenic fever	Chemotherapy
		Fluconazole	Esophageal	AIDS
		Micafungin	Candidemia	TPN
Aspergillus	Septate Hyphae Branch at 45° angles	Corticosteroids and itraconazole	ABPA	CF patients present like asthma
		Voriconazole	Aspergilloma	Previous cavitary lung lesion
		Voriconazole	Invasive aspergillosis	
Pneumocystis	Silver stain yeast	TMP/SMX	Interstitial pneumonia, hypoxemia	AIDS CD4 < 200
Cryptococcus	~~India ink~~ yeast *Crypto* Ag CSF	Amphotericin B and flucytosine	Crypto meningitis	AIDS CD4 < 100
Mucor	Nonseptate hyphae 90° branches	Amphotericin B	DKA, rhinocerebral infection	Diabetics, nasal septum, fungus

Table 1.2: Opportunistic Fungi Review